REMARKS

Claims 13-27 are pending in the instant application and under consideration.

I. The Amendments

The claims have been amended, without prejudice, for the purpose of more clearly defining what Applicants regard as the invention. The amendment does not add new matter, and is fully supported by the specification and the claims as originally filed. Entry pursuant to 37 CFR § 1.111 is respectfully requested.

II. Withdrawn Rejections

Applicants note with appreciation that the rejection of Claims 13-27 under 35 U.S.C. § 112, second paragraph, has been withdrawn.

Applicants further note with appreciation that the rejection under 35 U.S.C. § 112, first paragraph, has been withdrawn.

Applicants further note with appreciation that the rejection of Claims 13, 15, 17, 19, 20, 22, 24, and 26 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,004,797 ("Colosi") has been withdrawn.

Finally, Applicants note with appreciation that the rejection of Claims 5, 6, 8, and 9 (which should have been 13, 15, and 17-19) under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,872,005 ("Wang") has been withdrawn.

III. Informalities

Claims 13-27 are objected to because they us the abbreviation AAV. The claims have been amended to spell out the term *adeno-associated virus* the first time the abbreviation is used. The objection should therefore be withdrawn.

IV. The Rejections

A. The Rejection Of Claims 13-27 Under 35 U.S.C. § 112, Second Paragraph

Claims 13-27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The rejection is obviated and/or overcome in view of the amendment to the claims.

B. The Rejection Of Claims 13, And 17-19 Under 35 U.S.C. § 102(b)

Claims 13, and 17-19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Bett *et al.*, 1994, *Proceedings of the National Academy of Sciences* 91:8802-8806 ("Bett"). The rejection is respectfully traversed.

The standard governing anticipation under 35 U.S.C. § 102 is one of strict identity (*see* M.P.E.P. § 2131). A cited reference must meet each claim limitation in order to constitute anticipation. Applicants submit that this strict standard of identity has not been met because the cited reference does not teach a fusion protein comprising a carrier or vehicle with no detectable immunogenic effect and one or a plurality of $CD8^+$ T-cell epitopes.

The rejected claims are directed to an adeno-associated virus (AAV) nucleic acid comprising an AAV helper virus sequence for developing AAV viral particles, wherein said AAV helper virus sequence comprises the complete adenovirus 5 sequence with exception of the E1 region, and to compositions comprising the same.

The Office Action characterizes Bett as teaching a sequence comprising the entire adenovirus type 5 with a deletion of the E1 region, and concludes that Bett anticipates the instant invention. Applicants respectfully disagree with that conclusion.

Applicants wish to point out that, contrary to what is asserted in the Office Action, Bett does not teach what is presently claimed, *i.e.*, an AAV nucleic acid comprising an AAV helper virus sequence for developing AAV viral particles, wherein said AAV helper virus

s quence comprises the complete adenovirus 5 sequence with exception of the E1 region. Therefore, Bett cannot anticipate any of the present claims.

In view of the above, the rejection of Claims 13, and 17-19 under 35 U.S.C. §102(b) as being anticipated by Bett is in error and should be withdrawn.

C. The Rejection Of Claims 13, 17-20, And 24 Under 35 U.S.C. § 103(a)

Claims 13, 17-20, and 24 are rejected under 35 U.S.C. § 103(a) as being obvious over Bett and United States Patent No. 6,004,797 by Colosi *et al.* ("Colosi"). The rejection is respectfully traversed.

In issuing a rejection under § 103(a), the Examiner bears the burden of citing references that establish a *prima facie* case of obviousness. The cited references do not establish a *prima facie* case of obviousness if they do not teach or suggest each of the claim limitations, do not motivate one to combine the references to achieve the claimed invention or do not provide a reasonable expectation of success in achieving the claimed invention (*see* M.P.E.P. §§ 706.02(j) and 2143; *see, e.g., In re Sernaker*, 217 USPQ 1 (Fed. Cir. 1983); *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985); *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988); *Panduit Corp. v. Denisson Manufacturing Co.*, 1 USPQ2d 1593, 1597 (Fed. Cir. 1987); *In re Nilssen*, 7 USPQ 2d 1500 (Fed. Cir. 1988)).

The rejected claims are directed to an adeno-associated virus (AAV) nucleic acid comprising an AAV helper virus sequence for developing AAV viral particles, wherein said AAV helper virus sequence comprises the complete adenovirus 5 sequence with exception of the E1 region, to compositions comprising the same, and to methods for producing an rAAV viral particle preparation which is not contaminated with helper viruses.

It is emphasized that Bett is not concerned with the production of AAV, but merely the construction of adenoviral vectors. In the present application, the production of AAV and recombinant AAV, respectively, is not carried out by an infection with adenoviral vector (*i.e.*,

viral particles), but with transfected adenoviral DNA. These DNA lack the L1 gene (which is required for the generation of capsid). Thus, the production of adenoviral particles might not contaminate the preparation of the AAV vector is not possible. This is one of the major advantages of the plasmids of the present application and this is not described in Bett. Furthermore, Bett does not teach that AAV sequences and the helper virus sequences with a deletion of E1 can be present on a single plasmid. In this context, we refer to the discussion on page 8805 of Bett as well as Fig. 3, showing that in Bett, for the preparation of AAV particles, the 293 cells were transfected with a plasmid containing all essential Ad5 sequences (with a deletion of E1) and in addition with a second plasmid which contains the packaging signal.

It is also noted that Colosi does not teach the use of a plasmid containing the AAV sequences as well as the helper virus sequences, let alone how to achieve this. Indeed, in the sections referred to by the Examiner (column 5, lines 5-57, column 8, lines 29-39 and column 17, lines 23-30), nowhere any hint can be found that the AAV sequences and the helper virus sequences should be combined on a single vector. Colosi always starts from the assumption that AAV sequences and AAV helper sequences have to be used for the transfection of a cell separately.

In view of the above the rejection under 35 U.S.C. § 103(b) over Bett and Colosi should be withdrawn.

CONCLUSION

In view of the above amendments and remarks, the subject application is believed to be in good and proper order for allowance. Early notification to this effect is earnestly solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (415) 781-1989. The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 50-2319 for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,
DORSEY & WHITNEY, LLP

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By: _____
Birgit Millauer, Reg. No 43,341

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Customer No.: 32940
Dorsey & Whitney LLP
Four Embarcadero Center, Suite 3400
San Francisco, California 94111-4187
Telephone: (415) 781-1989
Fax No. (415) 398-3249